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ABSTRACT

This study examined individual patterns of the maturation of auditory evoked potential (AEP) in normal infants to determine whether longitudinal data show less variability than cross-sectional data, and to further assess the effect of stage of sleep on AEP. The AEPs for 10 children were examined by repeated testing between the ages of about two weeks and three years. Responses during interstimulus intervals to clicks presented every 2.5 seconds via a loudspeaker to the sleeping child were recorded from electrodes at the vertex referred to joined mastoids. Analysis of the data confirmed earlier cross-sectional findings. General developmental age trends were found in response morphology from birth to three years. All children did show AEPSs to the intensity of the stimulus used in the study, indicating that the presence or absence of the AEPs is important for clinical diagnosis. Data tables are included. (Author/ED)

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Longitudinal Study of Averaged Auditory Evoked Potentials in Normal Children from Birth to Three Years of Age

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Sensory averaged potentials (EPs) reflect underlying neural development of the maturing child. In most research thus far which has been concerned with EP development in childhood, groups of children at different ages have been studied, or if a mixed longitudinal and cross-sectional design was used, developmental information on individual subjects has not been reported. Most researchers report considerable intersubject variability and measures of intra-subject variability have been based on short term -- usually within session-- consistencies and inconsistencies (e.g., Dustman and Beck, 1969; Ornitz et al. 1967, 1969; Tanguay et al. 1973; Barnet et al. 1971; Ellingson et al. 1973, 1974; Engel and Milstein, 1971). It has not thus far been reported to what extent the individual normal child conforms to the developmental trends which have been reported or whether individuals show characteristic response patterns which can be used as an index of individual development.

A recent report from this laboratory (Barnet et al. 1975) reported on the maturation of the auditory evoked potential (AEP) during sleep from the neonatal period to age three years. A total of 130 normal children were studied, ten in each group of thirteen separate age groups. Latencies of prominent peaks in the AEP were found to decrease with age, the most rapid decrease being in the first year. Measures of AEP amplitude also showed significant changes. AEP parameters were influenced not only by age but also by the child's state along the sleep/wake continum. Although highly significant age trends were discovered, variability was high especially at the younger ages.

The purposes of the present study were to examine individual patterns of AEP maturation, to determine whether longitudinal data would show less variability than the cross-sectional data, and to further assess the effect of stage of sleep on the AEP. To this end, we examined AEPs for ten normal children who were

tested repeatedly between the ages of about two weeks and three years. Nine of these children were represented once in the previously reported cross-sectional study (Barnet et al. 1975).

METHODS Subjects

Five girls and five boys were tested. Each participated in from ten to seventeen sessions, which took place at approximately bi-weekly intervals until six months, at three month intervals from six to eighteen months, and then at six month intervals until age three. All children missed recording sessions for various reasons, and in some cases the data were inadequate for technical reasons but each child is represented by at least nine recordings. There were six white and four black subjects. Six of the children were living at home and four resided in child care institutions during all or part of the time covered by this study.

All of the subjects had normal pediatric and neurological examinations and normal scores on the Bayley Test of Infant Development. Testing was done only when the child appeared to be in good physical health. Most of the children had acute middle-ear infections at least once during the three years of study. Although none of the children was tested while he was ill, we had no measures, other than the normal otoscopic exams, to corroborate normal hearing on the day of the AEP test.

Procedures

Recordings were made from an electrode at the vertex (Cz) referred to joined mastoids. Several sets of clicks at different intensities were presented via a loudspeaker to the child. The results for the response to the most intense click in the series, which was 65 dB HL* (108 dB SPL) will be given in this report.

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*Hearing levels are given in dB above averaged voluntary thresholds of five normal hearing adults measured under the conditions used for the children.

100 identical clicks were presented with an interstimulus interval of 2.5 seconds. The EEG during the first second interval following each click was averaged by means of a CAT computer. Details of the recording procedures are presented in Barnet et al. (1975). All the recordings were made while the children were sleeping; no sedation was used. Sleep stage was scored from the polygraph records using the criteria of Anders et al. (1971) for the younger ages and Rechtschaffen and Kales (1968) from about three months onward.

The parameters of the EP discussed in this report are the latencies to P_2, N_2, and P_3 and the peak to peak amplitudes between them (Fig. 1).

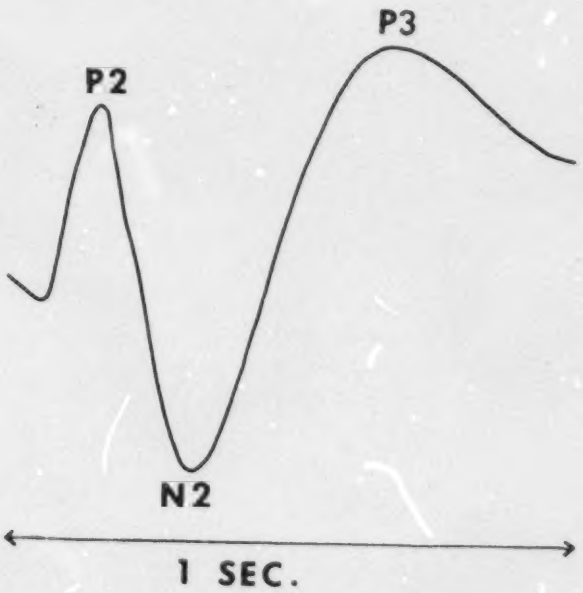

Fig. 1. Schematic representation of the AEP showing peaks discussed in this report. Peak to peak amplitudes between P_2 and N_2 and between N_2 and P_3 were measured as well as latencies from onset of the stimulus (at beginning of tracing) to each peak.

Micrometer measurements were made from X-Y plots of the responses and latencies and amplitudes calculated using a calibration factor. The P_2N_2 segment was used as the"landmark" for the response since it was the least ambiguous component. P_2 was defined as the most prominent positive peak (with respect to the mastoid reference), occuring with a post-stimulus latency of approximately 100 to 300 milliseconds. N_2 was defined as the lowest negative deflection following the P_2, occuring usually within the first 500 milliseconds. P_3 was the major positive wave following N_2 and usually was in the second half second following the stimulus. Results from N_0, P_1, N_1, P_{3A}, and P_{3B} will also be reported in the journal article covering this data.

RESULTS

Overall results for the whole group will be considered first. In order to show the relationship between the AEP components and age, regression lines were computed using the latency or amplitude measurement and log age. The overall results for the latency measures were decreases over age for all three measures, P_2, N_2, and P_3. These regression lines are seen in Fig. 2.

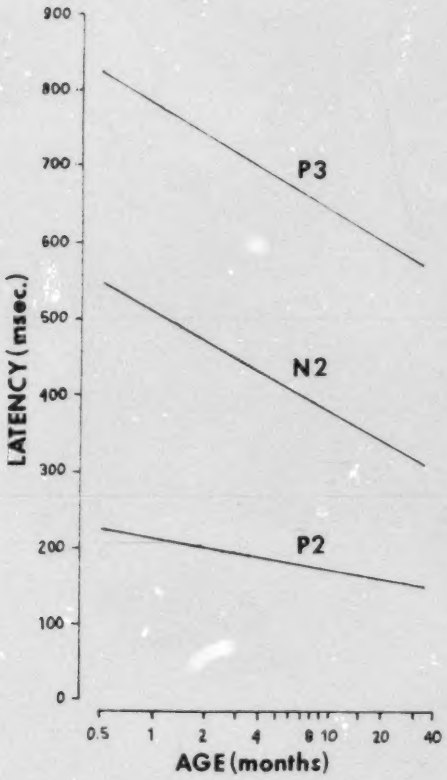

Figure 2. Regression lines for P_2, N_2 and P_3 latencies with respect to $\log_{10}$ age.

P_2 latency decreased from about 225 msec. at 0.5 months to 150 msec. at 36 months. Log age accounted for 27% of the variance in P2 latency (r=-.52). N_2 latency decreased from about 540 msec. at 0.5 months to 310 msec. at 3 years, and log age accounted for 34% of the variance in N_2 latency (r=.58). P_3 latency decreased from about 815 msec. at 0.5 month to 575 msec. at 3 years, and 20% of the variance was accounted for by log age. Both N_2 and P_3 latencies decreased at a greater rate over age than did P_2.

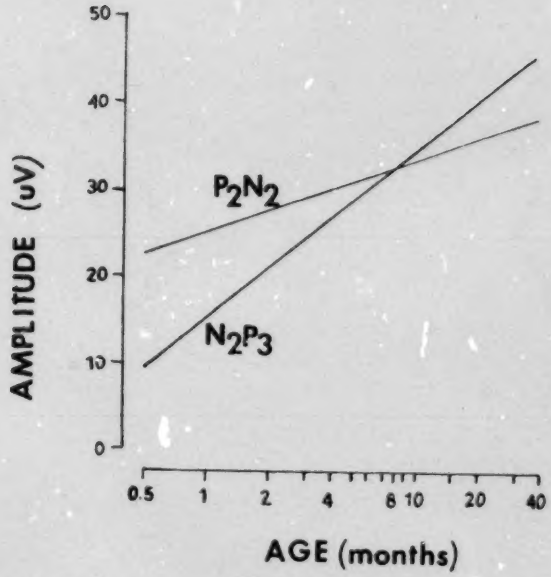

Figure 3. Regression lines for P_2N_2 and N_2P_3 amplitudes with respect to $\log_{10}$ age.

Figure 3 shows that amplitude for both P_2N_2 and N_2P_3 increased over age when all the recordings taken in all stages of sleep were considered. P_2N_2 increased from 23 uV at 0.5 month to 39 uV at 3 years. N_2P_3 increased from 10 to 46 uV. The greater increase in N_2P_3 with age, as compared with that of P_2N_2, demonstrates the growing prominence of the P_3 wave with increasing maturity. This changing morphology of the AEP with age is illustrated by the tracings from David and Traci, shown in Figure 4.

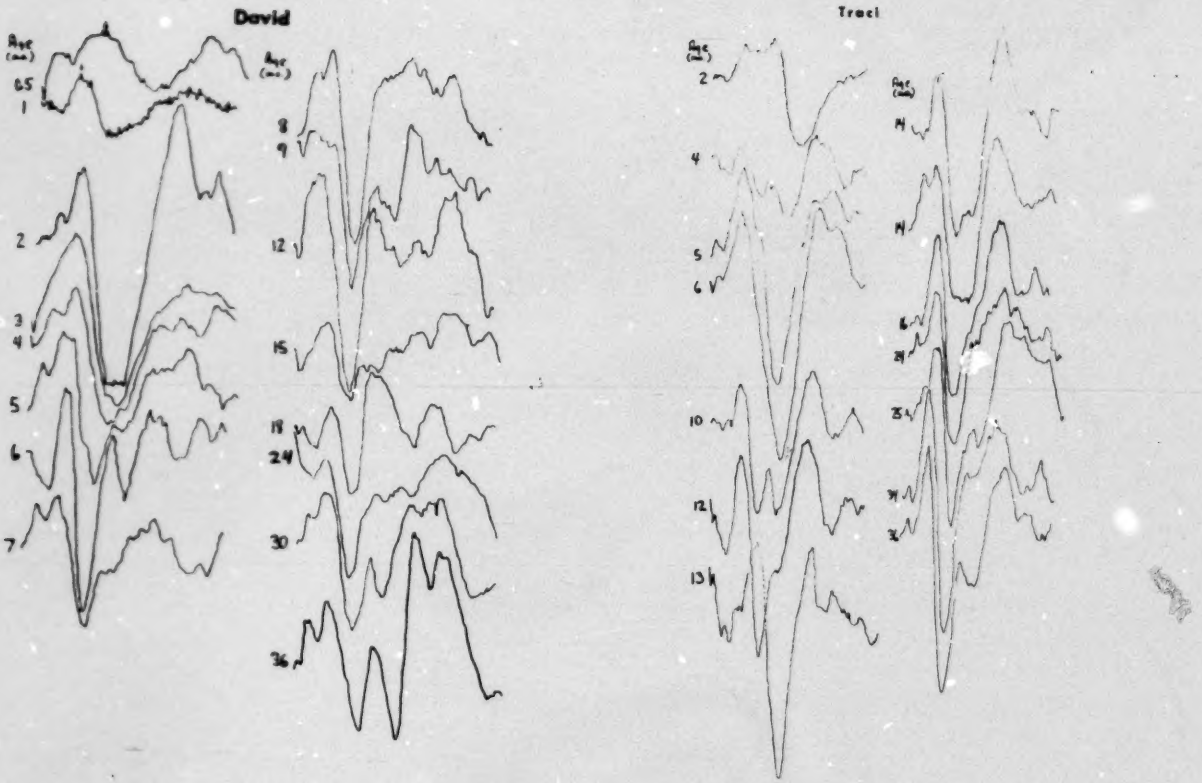

Figure 4. AEP tracings for two children. David (left) was tested 16 times between the ages of 0.5 mo. and 36 months. Traci (right) was tested 14 times between the ages of 2 and 36 months.

David at 0.5 and 1 month of age shows the rounded P_2 and P_3 waves which are often found in children under two months of age. The P_2N_2 and N_2P_3 amplitudes are very small compared with those found at older ages. David's 2 month tracing resembles those found more usually for Ss 6 months of age or older, i.e. the P_3 wave is prominent and the $P_2N_2P_3$ wave complex forms a "V" shape. His older tracings have prominent P_2 waves and prominent but broad complex P_3 waves (our P_{3B} type). Traci shows the rounded P_2 and P_3 waves in her 2 month tracing that are typical of very young infants, and after that shows her typical response -- 1 large clear "V" shaped $P_2N_2P_3$ component with no small waves or "shoulders" on the P_2N_2 wave and a large P_3 wave with a clearly defined sharp peak (our P_{3A} type).

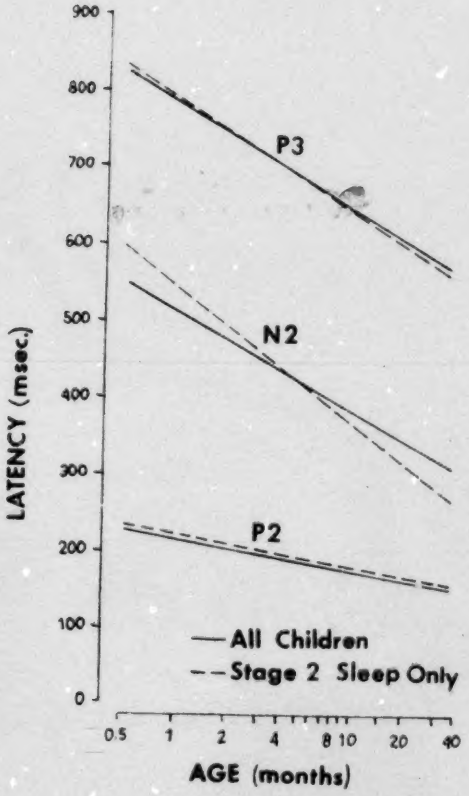

Figure 5. Regression lines with respect to $\log_{10}$ age for P_2, N_2 and P_3 latencies for all data in the study and for only those recordings done when the children were in stage 2 sleep.

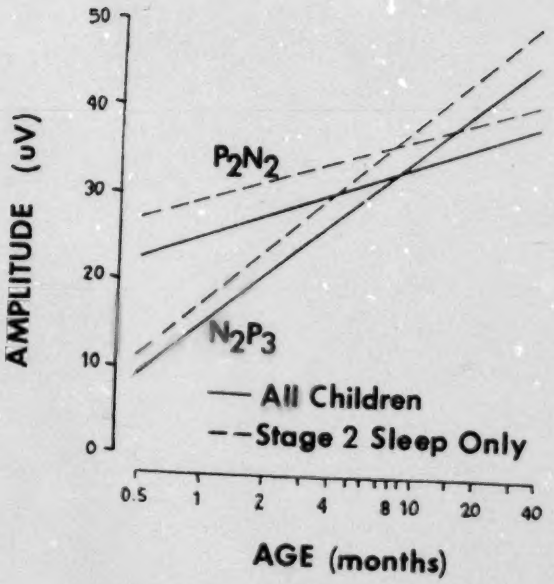

Figure 6. Regression lines with respect to $\log_{10}$ age for P_2N_2 and N_2-P_3 amplitudes for all data in the study and for only those recordings done when the children were in stage 2 sleep.

In order to look at the age effects independent of sleep stage, those recordings obtained during stage 2 sleep (or slow wave sleep for the neonates) were analyzed separately. Seventy-one recordings in stage 2 sleep were involved in this second analysis. The latency decreases over age all remained signiicant and the regression lines were quite similar to those determined for the overall data, as seen in Figure 5.

When only those children in stage 2 or slow wave sleep were considered, the increase in P_2N_2 amplitude over age was not significant; probably because of the decreased N (Fig. 6). The N_2P_3 amplitude increase did remain

significant, however. These results, i.e., N_2P_3 amplitude increase regardless of sleep stage and the P_2N_2 amplitude increase being a marginal effect, was also found in this laboratory's cross-sectional study of 130 children between the ages of 10 days and three years in which the same stimulus conditions were used (Barnet, et al. 1975).

The regression lines for the ten children in the present study were very similar to the regression lines for the previously studied cross-sectional group. The regression lines for the latency measures are almost superimposed (Fig. 7) and the slopes of the regression lines for amplitude are likewise very similar. Thus, the sample of ten children studied longitudinally seems to be fairly representative of the population of 130 children studied previously.

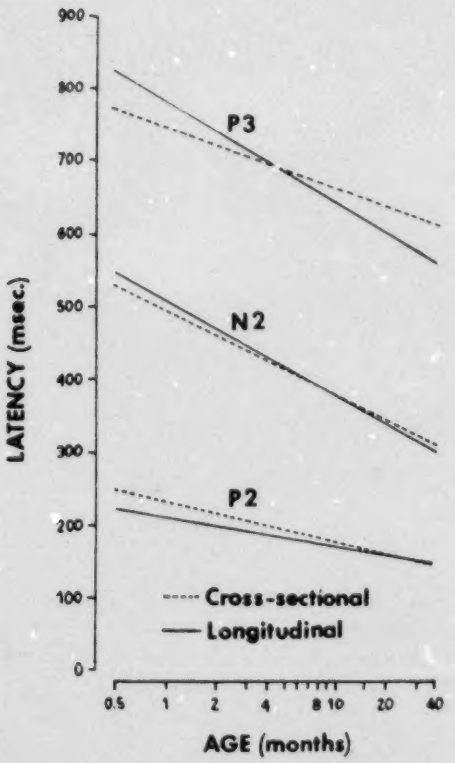

Figure 7. Regression lines for P_2, N_2 and P_3 latencies with respect to $\log_{10}$ age for the present longitudinal study and the previously reported cross-sectional study (Barnet et al. 1975).

Table 1 shows the percentage of the variance which was accounted for by age when the EP components were examined in the cross-sectional study (between subject variance) and in the longitudinal study (within subject variance). The figures for the longitudinal study are the median percentages of variance for individual subjects, since the overall figures presented at the bottom of Table 2 represent both between subject and within subject variance.

TABLE 1

Percentage of the variance for P_2, N_2 and P_3 latency and P_2N_2 and N_2P_3 amplitudes which was accounted for by age for the cross-sectional study (between subject variance, Barnet et al. 1975), and for the longitudinal study (within subject variance). The median percentage for the individual subjects in the longitudinal study is presented:

	LATENCY			AMPLITUDE	
	P_2	N_2	P_3	P_2N_2	N_2P_3
Between Subject (cross-sectional)	37	45	17	5	26
Within Subject (longitudinal)	42	44	28	27	29

Age accounts for a slightly greater percentage of the variance when that variance is found within subjects only, rather than between subjects. However, there is still over 50% of the variance which is still unaccounted for. The background EEG would account for some of this variability. Classification of the EEG into sleep stages has some effect in reducing the variance, but even when subjects in only a single sleep stage, stage 2 sleep, are considered, there is still a great deal of variability in the EP measures which is not age related. Since the sleep stage classifications are rather broad categories, a more refined method of classifying the background EEG may have to be utilized.

TABLE 2

Percents of variance in the EP measures listed below that were accounted for by log age

	LATENCY			AMPLITUDE	
	P2	N2	P3	P2N2	N2P3
Josh	50.8	16.9	3.6	34.5	39.4
Elaine	11.9	0.4	0.7	71.9	57.1
Zack	70.2	8.8	39.4	60.2	59.1
Mark	52.1	32.5	55.3	9.1	30.9
Bea	38.8	58.7	27.9	43.6	0.02
David	41.8	52.5	29.3	8.3	28.0
Vern	29.5	52.4	0.0	18.8	5.8
Patricia	42.4	43.3	26.3	17.9	15.9
Traci	7.6	81.7	59.3	20.4	37.0
Darnell	55.0	44.0	36.6	41.6	25.8
All 10 Children Combined	27.4	33.8	20.2	5.8	22.0

Each of the individual children showed a good relationship between at least one of their EP components and log age, but for no children were all of the EP components well related to age. Table 2 shows the percentages of the variance in the EP measures that were accounted for by log age for each of the ten children and also for all ten children combined. The higher the percent variance accounted for by age, the better the relationship between age and that EP component. N_2 latency was the measure which had the best relationship with age for all ten children combined; 34% of the N_2 variance was accounted for by age. For five of the children, N_2 latency showed the

best relationship with age of all the components examined.

For a given child, one of the EP components could show a very strong relationship with age, while another component had a very weak relationship. Eight of the children had one or two EP components which had 10% or less of the variance accounted for by age. For example, Zack's P_2 latency component decreased consistently with age, 70% of the variance in it being accounted for by age, but his N_2 latency was not age related, only 9% of the variance being accounted for by age. His amplitude components both had strong age relationships with about 60% of the variances being accounted for by age. Traci had a strong age relationship in her N2 latency measure (Fig. 5), 82% of the variance being accounted for by age, but her P2 latency was not strongly age related, only 8% of the variance being accounted for by age. Elaine showed virtually no age relationship in her latency measures, but both the P_2N_2 and N_2P_3 amplitude measures showed strong age relationships, 72% and 57% of these respective variances being accounted for by age.

In spite of the large amount of variability found in the EP measures, there are consistencies within many children from one testing to another as to the form of their response, e.g., Traci's large clear "V" shaped $P_2N_2P_3$ components which did not contain complex waves. David had a negative (N_1) consistently preceding his P_2 wave and had a very broad complex P_3 wave. Elaine (Fig. 8) had consistent but complex responses.

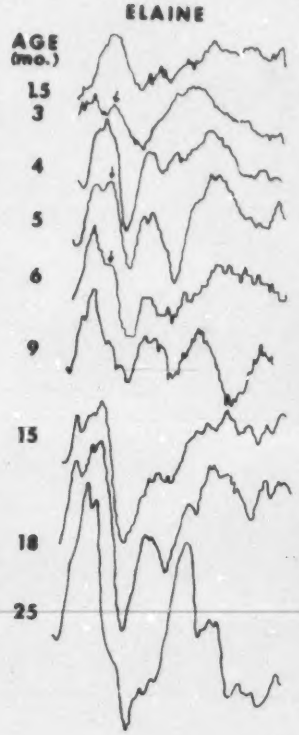

Figure 8. AEP tracings for Elaine

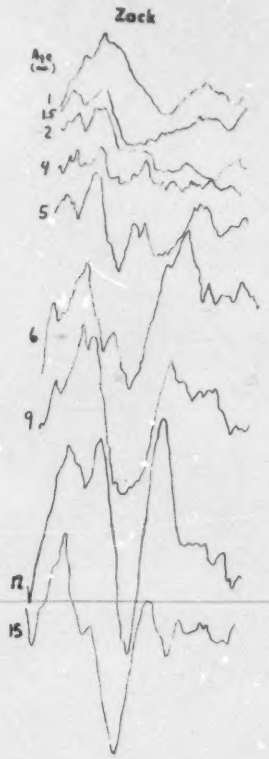

Figure 9. AEP tracings for Zack

Her P_2 waves usually had double peaks or shoulders and her P_3 waves had a complex sawtooth appearance. It is visually apparent that her peak latencies do not change with age, but her responses do get larger, as results shown by the percent variance accounted for by age. Zack (Fig. 9) shows the typical rounded responses at his early ages. His last four tracings, from 6 to 15 months, show the prominent $P2N_2$ P_3 "V" form and are similar to each other in that they have either shoulders on the P_2N_2 wave or double peaks on the P_2 wave.

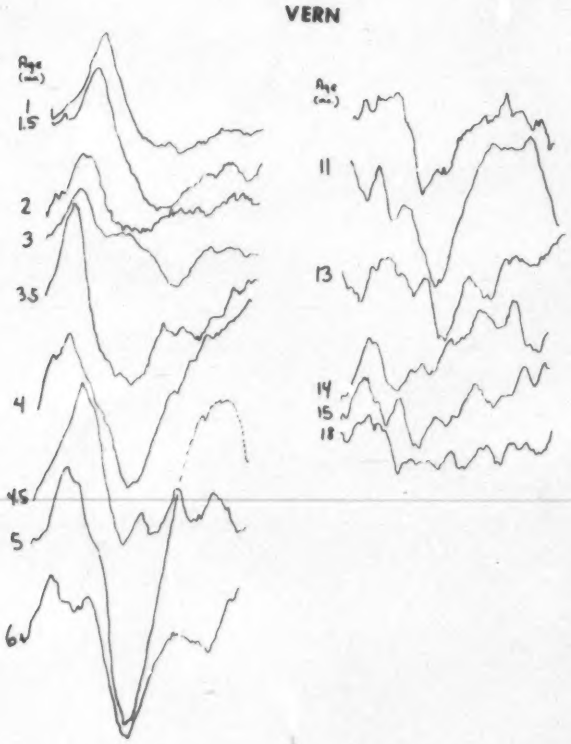

Fig. 9. AEP tracings for Vern.

Not all children show such consistent response morphology. Vern (Fig. 9) shows a very clear P_2N_2 response at age one month. By six months the P_2 wave has a double peak or saw tooth appearance. His EP continues to become more complex as he gets older. Sleep stage itself does not explain the changing response form, but perhaps some other measure of the background EEG might be better related to the changing response. The fact that we are averaging 100 responses, may also contribute to a great deal of variability, since if

the EP is not perfectly time-locked to the stimulus, the averaged potential may not look like any of the individual responses. Some children may show greater variability in the latency of their individual responses than other children, and perhaps this would lead to more complex averaged responses.

SUMMARY

These longitudinal data confirm our earlier cross-sectional findings that in the AEP of sleeping infants, the P_2, N_2, and P_3 latencies decreased with log age and the N_2P_3 amplitude increased with log age. The increase in P_2N_2 amplitude was only a marginal effect in both studies. It was surprising, however, that there seemed to be nearly as much variability in the longitudinal data as in the cross-sectional. In some children, one response component is clearly age related in its changes, while another response component in the same child showed little or no relationship to age. There was a great deal of variability in response morphology between children, although some children showed very consistent response forms from one age to another.

There were general developmental age trends in response morphology from birth to three years. For example, the younger infants tended to have long latencies and small rounded peaks for their P_2 and P_3 waves, and older children had prominent $P_2N_2P_3$ "V" shapes with a steep N_2P_3 slope and sharp P_3 peak or a large, broad P_3 peak. Extreme responses might suggest that one should examine a child more closely, e.g., it would be very unusual for a normal three year old to have the long latency, small rounded P_2 wave and lack of a large, clear P_3 wave that it typical of infants under two

months of age, but extreme responses in and of themselves cannot yet be used for a definitive clinical decision about a child. All normal children did show AEPs to the intensity of stimulus used in this study. The fact that the AEPs should be present means that the presence or absence of the AEPs is important for clinical diagnosis, as in the application of AEPs to audiometry.

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